Derivatives of carboxylic acids, their preparation and medicaments containing them.

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Abstract of **EP0023569**

1. Claims (for the Contracting States : BE, CH, DE, FR, GB, IT, LI, LU, NL, SE) Carboxylic acid amides of general formula I see diagramm : EP0023569,P97,F1 wherein R represents a hydrogen, chlorine or bromine atom or a cyclic alkyleneimino group with 4 to 7 carbon atoms in the imino ring ; R1 represents a hydrogen, fluorine, chlorine or bromine atom ; an alkyl or alkoxy group with 1 to 6 carbon atoms ; an alkoxy group with 1 to 3 carbon atoms substituted by a phenyl group ; a hydroxy, nitro, amino, cyano or carboxy group ; an alkanoylamino, alkoxycarbonyl or dialkylamidosulphonyl group, wherein the alkyl part may contain 1 to 3 carbon atoms ; R2 and R3 , which may be the same or different, represent alkyl groups with 1 to 7 carbon atoms, alkenyl groups with 3 to 7 carbon atoms, cycloalkyl groups with 3 to 7 carbon atoms, alkyl groups with 1 to 3 carbon atoms substituted by a phenyl group, or phenyl or adamantyl groups, or R2 and R3 together with the nitrogen atom between them represent an unbranched alkyleneimino group with 3 to 12 carbon atoms in the imino ring, an unbranched alkyleneimino group with 4 to 6 carbon atoms in the imino ring which may be substituted by one or two alkyl groups each with 1 to 4 carbon atoms, an alkoxy group with 1 to 3 carbon atoms, a hydroxy, phenyl, carboxy or alkoxycarbonyl group with a total of 2 to 4 carbon atoms and/or wherein a methylene group is replaced by an imino group (which may be substituted by an alkyl group with 1 to 3 carbon atoms, an alkoxycarbonyl group with a total of 2 to 4 carbon atoms, a phenyl, halophenyl, benzyl, pyridyl or furoyl group), by an oxygen or sulphur atom or by a carbonyl, sulphoxide or sulphonyl group ; a saturated or partially unsaturated

azabicycloalkyl group with 7 to 10 carbon atoms, a piperidino group substituted in the 3- and 5-positions by a total of 3 or 4 alkyl groups each with 1 to 3 carbon atoms ; a 1,4-dioxa-8-aza-spiroalkyl group with 6 to 9 carbon atoms, or a pyrrolyl or tetrahydropyridino group ; R4 represents a hydrogen atom or an alkyl group with 1 to 3 carbon atoms ; Y represents an oxygen atom, an imino group or a methylene group optionally substituted by one or two alkyl groups each having 1 to 3 carbon atoms, Z represents a hydrogen or halogen atom, a carboxy, cyano, formyl, hydroxymethyl, hydroxycarbonylethylene, nitro, amino, allyloxycarbonyl, phenoxycarbonyl, benzyloxycarbonyl or phenylethoxycarbonyl group, an alkoxycarbonyl group with a total of 2 to 8 carbon atoms, a cycloalkoxycarbonyl group with a total of 4 to 8 carbon atoms, a methyl group optionally substituted by 2 or 3 alkoxy groups or by a carboxy, alkoxycarbonyl or ethylenedioxy group, wherein the alkoxy group may contain 1 to 3 carbon atoms ; an acetyl group, optionally substituted by a carboxy group or alkoxycarbonyl group with a total of 2 to 4 carbon atoms ; an ethyl or ethylene group substituted by one or two alkoxycarbonyl groups each having a total of 2 to 4 carbon atoms, or by two carboxy groups ; an aminocarbonyl group optionally mono- or di-substituted by an alkyl group with 1 to 7 carbon atoms, a cycloalkyl group with 3 to 7 carbon atoms and/or an alkenyl group with 3 to 7 carbon atoms ; a piperidinocarbonyl, morpholinocarbonyl, thiomorpholinocarbonyl or N-alkyl-piperazinocarbonyl group wherein the alkyl group may contain 1 to 3 carbon atoms ; or an ethyl group substituted by a carboxy group if the groups R2 and R3 together with the nitrogen atom between them represent one of the above-mentioned cyclic imino groups, and the physiologically acceptable salts thereof with inorganic or organic acids and also bases if Z represents or contains a carboxy group. 1. Claims (for the Contracting State AT) Process for the preparation of new carboxylic acid amides of general formula I see diagramm : EP0023569,P104,F1 wherein R represents a hydrogen, chlorine or bromine atom or a cyclic alkyleneimino group with 4 to 7 carbon atoms in the imino ring ; R1 represents a hydrogen, fluorine, chlorine or bromine atom ; an alkyl or alkoxy group with 1 to 6 carbon atoms ; an alkoxy group with 1 to 3 carbon atoms substituted by a phenyl group ; a hydroxy, nitro, amino, cyano or carboxy group ; an alkanoylamino, alkoxycarbonyl or dialkylamido-sulphonyl group, wherein the alkyl part may contain 1 to 3 carbon atoms ; R2 and R3 , which may be the same or different, represent alkyl groups with 1 to carbon atoms, alkenyl groups with 3 to 7 carbon atoms, cycloalkyl groups with 3 to 7 carbon atoms, alkyl groups with 1 to 3 carbon atoms substituted by a phenyl group, or phenyl or adamantyl groups, or R2 and R3 together with the nitrogen atom between them represent an unbranched alkyleneimino group with 3 to 12 carbon atoms in the imino ring, an unbranched alkyleneimino group with 4 to 6 carbon atoms in the imino ring which may be substituted by one or two alkyl groups each with 1 to 4 carbon atoms, an alkoxy group with 1 to 3 carbon atoms, a hydroxy, phenyl, carboxy or alkoxycarbonyl group with a total of 2 to 4 carbon atoms and/or wherein a methylene group is replaced by an imino group (which may be substituted by an alkyl group with 1 to 3 carbon atoms, an alkoxycarbonyl group with a total of 2 to 4 carbon atoms, a phenyl, halophenyl, benzyl, pyridyl or furoyl group), by an oxygen or sulphur atom or by a carbonyl, sulphoxide or sulphonyl group ; with 7 to 10 carbon atoms, a piperidino group substituted in the 3- and 5-positions by a total of 3 or 4-alkyl groups each with 1 to 3 carbon atoms ; a 1,4-dioxa-8-aza-spiroalkyl group with 6 to 9 carbon atoms, or a pyrrolyl or tetrahydropyridino group ; R4 represents a hydrogen atom or an alkyl group with 1 to 3 carbon atoms ; Y represents an oxygen atom, an imino group or a methylene group optionally substituted by one or two alkyl groups each having 1 to 3 carbon atoms, Z represents a hydrogen or halogen atom, a carboxy, cyano, formyl, hydroxymethyl, hydroxycarbonylethylene, nitro, amino, allyloxycarbonyl, phenoxycarbonyl, benzyloxycarbonyl or phenylethoxycarbonyl group, an alkoxycarbonyl group with a total of 2 to 8 carbon atoms, a cycloalkoxycarbonyl group with a total of 4 to 8 carbon atoms, a methyl group optionally substituted by 2 or 3 alkoxy groups or by a carboxy, alkoxycarbonyl or ethylene-dioxy group, wherein the alkoxy group may contain 1 to 3 carbon atoms ; an acetyl group, optionally substituted by a carboxy group or alkoxycarbonyl group with a total of 2 to 4 carbon atoms ; an ethyl or ethylene group substituted by 1 or two alkoxycarbonyl groups each having a total of 2 to 4 carbon atoms, or by two carboxy groups ; an aminocarbonyl group optionally mono- or di-substituted by an alkyl group with 1 to 7 carbon atoms, a cycloalkyl group with 3 to 7 carbon atoms, a cycloalkyl group with 3 to 7 carbon atoms and/or an alkenyl group with 3 to 7 carbon atoms ; a piperidinocarbonyl, morpholinocarbonyl, thiomorpholinocarbonyl or N-alkyl-piperazinocarbonyl group wherein the alkyl group may contain 1 to 3 carbon atoms ; or an ethyl group substituted by a carboxy group if the groups R2 and R3 together with the nitrogen atom between them represent one of the above-mentioned cyclic imino groups, and the physiologically acceptable salts thereof with inorganic or organic acids and also bases if Z represents or contains a carboxy group, characterised in that a) an aminobenzoic acid of general formula II see diagramm : EP0023569,P105,F1 wherein R, R1 , R2 and R3 are as hereinbefore defined, or a reactive derivative thereof, optionally prepared in the reaction mixture, is reacted with an amine of general formula III see diagramm : EP0023569,P105,F2 wherein R4 , Y and Z are as hereinbefore defined, or with an N-activated amine of general formula III optionally formed in the reaction mixture, if an aminobenzoic acid of general formula II

is used and if Z in an N-activated amine of general formula III does not contain any carboxy or amino groups, or b) in order to prepare compounds of general formula I wherein R1 has the definitions given hereinbefore, with the exception of the hydroxy and amino group, and Y represents a methylene group optionally substituted by one or two alkyl groups each having 1 to 3 carbon atoms, a compound of general formula IV see diagramm : EP0023569,P105,F3 wherein R, R4 and Z are as hereinbefore defined, R1 and Y are defined as above and E represents a halogen atom, is reacted with an amine of general formula V see diagramm : EP0023569,P105,F4 wherein R2 and R3 are as hereinbefore defined, or c) in order to prepare compounds of general formula I wherein Z represents a carboxy group and Y does not represent an NH group a compound of general formula VI see diagramm : EP0023569,P105,F5 wherein R and R1 to R4 are as hereinbefore defined, Y has the meanings given hereinbefore with the exception of the NH group and A represents a group which can be converted into a carboxy group by oxidation, is oxidised or d) in order to prepare compounds of general formula I wherein Z represents a carboxy group, a compound of general formula VII see diagramm : EP0023569,P106,F1 wherein R, R1 to R4 and Y are as hereinbefore defined and B represents a group which can be converted into a carboxy group by hydrolysis, is hydrolysed, or e) in order to prepare compounds of general formula I wherein R2 represents an alkyl group with 1 to 7 carbon atoms, a cycloalkyl group with 3 to 7 carbon atoms, an alkyl group with 1 to 3 carbon atoms substituted by a phenyl group, or an alkenyl group with 3 to 7 carbon atoms, R3 represents an alkyl group with 1 to 7 carbon atoms, a cycloalkyl group with 3 to 7 carbon atoms, an alkenyl group with 3 to 7 carbon atoms, an alkyl group with 1 to 3 carbon atoms substituted by a phenyl group, or an adamantyl group, or R2 and R3 together with the nitrogen atom between them represent a 5- to 7-membered alkyleneimino ring, a piperidino group

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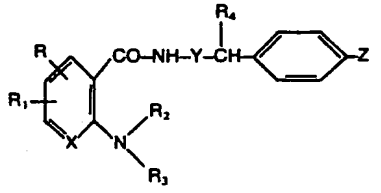
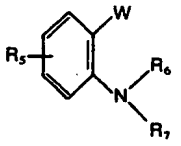
(54) **Neue Carbonsäurederivate, deren Herstellung und sie enthaltende Arzneimittel.**

(57) Neue Carbonsäure-Derivate der allgemeinen Formel



(I)

und neue 2-Amino-benzoesäure-Derivate der allgemeinen Formel



(Ia)

worin R, R_1 bis R_4, X, Y und Z die in Patentanspruch 1 sowie R_5–R_7 und W die in Patentanspruch 14 angegebene Bedeutung haben, und deren Säureadditionssalze, welche eine Wirkung auf den Stoffwechsel aufweisen. Außerdem stellen die neuen Verbindungen der allgemeinen Formel Ia sowie die Verbindungen der allgemeinen Formel I, in der Z ein Wasserstoff- oder Halogenatom, eine Nitro-, Amino- oder Cyanogruppe bedeutet, wertvolle Zwischenprodukte zur Herstellung der übrigen Verbindungen der allgemeinen Formel I dar, welche insbesondere blutzuckersenkende Eigenschaften besitzen.

Die Verbindungen der allgemeinen Formeln I und Ia können nach für analoge Verbindungen üblichen Verfahren hergestellt werden.

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